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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/590,375	06/09/2000	Keiji Endo	2173-0120P	2206

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EXAMINER	
SLOBODYANSKY, ELIZABETH	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 07/30/2002 15

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/590,375	Applicant(s) ENDO ET AL.	
	Examiner Elizabeth Slobodyansky	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 May 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) *7-9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The amendment field may 13, 2002 amending claims 1-6 has been entered.

Claims 1-10 are pending. Claims 7-9 are withdrawn. Claims 1-6 and 10 are under consideration.

Drawings

The drawings filed concurrently with the application have been objected by Draftsman, please refer to the attached PTO-948 form for details.

Claim Objections

Claim 6 is objected to because of the following informalities: on line 8 "and" instead of "or" should be typed. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5 and 6 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 5 and 6 are drawn to a mutant α-amylase obtained by introducing at least two mutations in SEQ ID NO:1 or a sequence that is at least 70% homologous to SEQ ID NO:1, wherein said mutant α-amylase possesses increased heat resistance and maintains resistance to chelating agents when compared to SEQ ID NO:1. Since the number of mutations is not limited, this amounts to any structure that is not necessarily homologous to SEQ ID NO:1.

Thus, the claims are drawn to an enormous genus of mutant α-amylases characterized only by function.

The specification discloses specific mutants of SEQ ID NO:1 mutated at the specific positions recited in the claims and specific combinations thereof. These mutations represent less than 1% of the structure of SEQ ID NO:1.

The specification fails to describe any other representative species by any identifying characteristics or properties other than the "functionality" of being a mutant α-amylase with the requisite properties and fails to provide any structure: function correlation present in all members of the claimed genus.

Therefore, the specification is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus.

Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Claims 1-6 and 10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a mutant α-amylase obtained by a specific disclosed substitution at single positions selected from the group consisting of position 11, 16, 49, 84, 144, 167, 169, 178, 188, 190, 205 and 209 in SEQ ID NO:1, specific multiple mutants mutated at positions 167/169, 190/209, 144/190/209, 16/144/190/209, 167/169/190/209, 107/167/169/190/209, 49/107/167/169/190/209, 49/107/205/167/169/190/209 of SEQ ID NO:1 and a hybrid α-amylase comprising residues 1-21 of SEQ ID NO:2 linked to residues 20-480 of SEQ ID NO:1 and said hybrid comprising specific mutations 167/169/190/209, wherein said mutants have increased heat resistance and maintain resistance to chelating agents when compared to SEQ ID NO:1, does not reasonably provide enablement for a mutant α-amylase having 70% or less homology thereto with said mutations and for other multiple mutations of SEQ ID NO:1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claims 1-6, 10 are so broad as to encompass any mutant α-amylase having 70% homology to SEQ ID NO:1 in which the amino acid corresponding to the above positions in SEQ ID NO: 1 having the requisite properties. As discussed above, claims 5 and 6 are not limiting the percent homology to 70% and encompass mutants with possibly very low homology to SEQ ID NO:1. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of mutant α-amylases broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the amino acid sequence of a single α-amylase.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is

unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass any α-amylase with 70% homology to SEQ ID NO:1 and the requisite properties in which the amino acid corresponding to residues recited above are mutated because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting α-amylase activity; (B) the general tolerance of amylases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any α-amylase residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of amino acid modifications of any α-amylase with 70% homology to SEQ ID NO:1 in which the amino acid corresponding to residues recited above in SEQ ID NO:1 are mutated. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of mutant α-amylases

having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim 10 is rejected as dependent from claim 1.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5 is confusing as reciting "at least one amino terminal sequence from 1st Asp through 11th Tyr or 100th Asp". It is unclear whether sequences other than sequence 1-11 or sequence 1-100 are encompassed rendering the metes and bounds of the claim unclear.

Allowable Subject Matter

Claim 6 would be allowable if rewritten in independent form and amended to recite a mutant consisting of (not comprising) the first and second mutations.

Response to Arguments

Applicant's arguments filed May 13, 2002 have been fully considered but they are not persuasive.

Applicants argue that references cited in the previous Office action as art in 103(a) rejections do not disclose α-amylases having amino acid sequences at least 70% homologous to SEQ ID NO:1. This is correct. However, the references were used in 103 rejections not 102 and only have to make the invention obvious. It would have been obvious to mutate some of the positions in SEQ ID NO:1 in view of the references. However, it is unpredictable whether the resulting mutants would have the properties required by the amended claims.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky whose telephone number is (703) 306-3222. The examiner can normally be reached Monday through Friday from 9:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX phone number for Technology Center 1600 is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Center receptionist whose telephone number is (703) 308-0196.

E. Slobodyansky

Elizabeth Slobodyansky, PhD
Primary Examiner

July 26, 2002